

REMARKS

This paper is responsive to the Office Action mailed June 3, 2004. Claims 15-34 are currently under examination.

On January 6, 2004 Applicants filed a response pursuant to 37 C.F.R §1.111, followed by a supplemental response filed on March 5, 2004. On May 6, 2004, Applicants' representatives received a telephone call from the Examiner during which the Examiner indicated that method Claims 15-27 were considered allowable, but that Claims 28-34, directed to kits and extraction buffers adapted for use in the claimed methods, were to be restricted from the application. On May 7, 2004, Applicants' representatives contacted Examiner Katcheves and proposed amending Claim 32. The Examiner indicated that the proposed amendment would place Claims 32-34 in form for allowance. The Examiner indicated that Claims 28-31 would be cancelled via an Examiner's amendment and a Notice of Allowance would issue shortly, indicating Claims 15-27 and 32-34 as allowed. Some two weeks later Applicants' representatives received another communication from the Examiner in which she advised that the earlier proposal for allowance had been withdrawn after review by her supervisory examiner. Accordingly, no amendments to Claims 32-34 have been entered and a second Office Action has been issued.

Claims 15 and 28 have been amended herein to specify the extraction buffer has a pH from 3 to 7. Support for the amendment is apparent from the original claim and throughout the specification, e.g., see page 3, lines 27-29.

Response to issues presented under obviousness-type double patenting

Claims 15-34 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1, 17, 19-21, 26, 27 and 32-34 of U.S. Patent No. 6,084,091 in view of Wan et al., *Analytical Biochemistry*, Vol. 223: 7-12 (1994). Specifically, the Examiner contends that although the claims are not identical, they are not patentably distinct. The Examiner reasons:

"It would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate nucleic acids by contacting the sample with a buffer having a pH from about 2 to about 8, as taught by the '091 patent, and a salt concentration of at least about 100 mM and comprising the extraction buffer and sample to a potato flour adsorption matrix as taught by the '091 patent and isolating the nucleic acid. One of skill in the art would have been motivated to optimize the salt concentration of the '091 patent because optimization of amounts in (sic) well-within the

purview of the ordinary skilled artisan. According to MPEP 2144.05: "differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Moreover, Wan et al., actually teach a buffer comprising PVP and 160 mM KCl. One of ordinary skill in the art would have been motivated to use PVP in a buffer which (sic) because of the increased yield and quality of nucleic acids it provides." (Office Action, page 4.)

Applicants respectfully traverse. Obviousness-type double patenting involves rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly owned patent. MPEP §804(II)(B)(1). The mere fact that a previous patent dominates, as in the case of improvements, a later patent does not in itself necessitate a double patenting rejection. As noted in the MPEP:

"Domination and double patenting should not be confused. They are two separate issues. One patent or application "dominates" a second patent or application when the first patent or application has a broad or generic claim which fully encompasses or reads on an invention defined in narrower or more specific claim in another patent or application. Domination by itself, i.e., in the absence of statutory or nonstatutory double patenting grounds, cannot support a double patenting rejection." MPEP §804(II).

The '091 patent claims a method of purifying, stabilizing, and isolating nucleic acids in a biological sample, including stool, wherein an adsorption matrix is added to the nucleic acid containing biological sample in order to bind contaminants. By using the inventive method taught in the '091 patent, substances which either contaminate or damage the nucleic acids, or inhibit the enzymatic manipulation thereof, are largely removed, allowing extended storage times for the nucleic acids. Nowhere in the '091 patent is a pH of 2-8 taught or suggested, as alleged by the Examiner in the above-quoted passage from the Office Action (i.e., "...contacting the sample with a buffer having a pH from about 2 to about 8, as taught by the '091 patent"). Similarly, contrary to the Examiner's statement, there is no teaching or suggestion of using a buffer with a salt concentration of "at least about 100 mM" in the '091.

Extraction buffers containing the presently claimed ingredients were neither taught nor suggested in the '091 patent, which teaches extraction buffers:

"[S]uitable to take up a specimen containing nucleic acids is a buffer system based on tris-HCL pH 8.5-9.5, EDTA and maybe NaCl. A particularly preferred buffer, especially for taking up stool specimens, contains 500mM (=500 mmol/l) tris-HCL pH 9, 50 mM EDTA and 10mM NaCl." (U.S. Pat. No. 6,084,091, column 5, lines 9-14.)

In contrast, the present invention involves the discovery that the nucleic acid isolation processes described in the above Muller references are more effective when combined with the particular buffer solutions described in the present application. Because the claimed method utilizing the novel buffer solutions is patentably distinct from the cited reference, i.e., the use of the buffer in the method resulted in a surprisingly unexpected increase in efficiency, the claims of the present invention are patentably distinct from the teaching of the '091 patent.

For example, Applicants teach that using an extraction buffer having: an acidic to neutral pH, with a preferred pH of 3-7, and a pH of 4-6.5 being particularly preferred; a high salt concentration, with a concentration of 100mM or greater being preferred; and a phenol-neutralizing substance, e.g., polyvinylpyrrolidone, β -mercaptoethanol and dithiothreitol.

Moreover, Applicants present direct comparison evidence showing the surprisingly dramatic increase in the amplifiability of the DNA isolated from stool when substituting the extraction buffer of the '091 patent with the extraction buffer taught in the present application, *see, e.g.* Examples 1 and 2 of Applicants' specification.

Incorporation of the extraction buffer taught in the present application into the DNA isolation method resulted in a surprisingly unexpected increase in efficiency. Therefore, the claims of the present invention are patentably distinct from the claims of the '091 patent.

The Examiner asserts that the deficiencies of the '091 teaching is overcome by its combination with Wan et al., noting:

"Wan et al. teach methods for isolating acids comprising using buffer adjuvants that significantly impact yield and quality of nucleic acids. Of the buffer adjuvants tested polyvinylpyrrolidone produced the best results. The extraction buffer was supplemented with PVP and additionally 160 mM potassium chloride, KCl, was added to the buffer." (Office Action, page 4.)

When combining references in and obviousness-type double patenting rejection, the MPEP states:

"A double patenting rejection of the obviousness-type is "analogous to [failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. **Therefore, any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination.**" MPEP §804(B)(I). (Emphasis added, internal citations omitted.)

In rejecting the claims as obvious over the combination of the '091 patent and Wan et al., the Examiner is illogically imputing a motivation on the part of the skilled artisan *to combine* the teachings. However, this conclusion is neither taught nor suggested in the prior art of record.

Applicants note the well-established standard regarding combining references as a basis for rejections claims as *prima facie* obvious. Obviousness cannot be established using Applicants' own disclosure as a guide to merely selecting and reconstructing the claimed invention from elements in the prior art:

"When the references are in the same field as that of the applicant's invention, knowledge thereof is presumed. However, the test of whether it would have been obvious to select specific teachings and combine them as did the applicant must still be met by *identification of some suggestion, teaching, or motivation in the prior art, arising from what the prior art would have taught a person of ordinary skill in the field of the invention.*" *In re Dance*, 160 F.3d 1339, 1348, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (emphasis added).

Omitting a particular statement of the suggestion or motivation to combine prior art references to make a claimed invention simply amounts to hindsight reconstruction based on an inventor's own teachings. As the Court of Appeals for the Federal Circuit noted in *In re Dembicczak*:

"Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability -- the essence of hindsight." *In re Dembicczak*, 175 F.3d 994, 999; 50 USPQ2d 1614, 1617; 1999 WL 246572 (Fed.Cir. 1999).

Wan et al. disclose an improved method to isolate RNA from recalcitrant plant species. Wan et al. researched the effect of a variety of buffers used in a hot borate RNA isolation procedure, noting:

"Of the buffer adjuvants evaluated, polyvinylpyrrolidone-40 (PVP-40) exhibited the single, most significant impact on the yield and quality of the RNA isolated from cotton leaves." (Wan et al., Abstract.)

In attempting to combine the references, the Examiner states reasons:

"One of ordinary skill in the art would have been motivated to use PVP in a buffer which (sic) because of the increased yield and quality of nucleic acids it provides." (Office Action, page 4.)

However, the Examiner fails to note that Wan et al., besides being directed to a wholly irrelevant process, actually teaches away from the present application, concluding that:

"Comparison of RNA isolated by modified borate buffers demonstrated that a hot borate buffer at **alkaline pH** and PVP-40 are sufficient to alleviate interference by polyphenolics and result in the recovery of high-quality RNA from recalcitrant plant species." (Wan et al., Results and Discussion, page 11.)

MPEP §2143.03 states that "[t]o establish *prima facie* obviousness of a claimed invention, all claim limitations must be taught or suggested by the prior art." Applicants note that neither of the references, alone or in combination, teaches or suggests a buffer particularly suited for the claimed methods having *an acidic to neutral pH*, a high salt concentration, and a phenol-neutralizing substance. In fact, both references cited *teach away* from the present invention, indicating that *alkaline* buffers are preferred. Applicants submit that the cited references actually support separate patentability of the present application, as Applicants clear departure from the teachings in the art led to the discovery that incorporation of the extraction buffer taught in the present application into the DNA isolation method resulted in a surprisingly unexpected increase in efficiency.

Applicants have amended the claims herein to further clarify the patentable distinctions over the art, i.e., Claims 15 and 28 have been amended to specify the extraction buffer has a pH from 3 to 7.

Because the methods of the present invention possess advantageous and unexpected properties that could not have been perceived or imagined by those skilled in the art from consideration of the '091 patent and Wan et al., and because the Examiner is unable to point to any suggestion in the art to combine the two teachings or to expect the novel results, Applicants request reconsideration and withdrawal of the rejection of Claims 15-34 under the judicially created doctrine of obviousness-type double patenting.

Response to issues presented under 35 U.S.C. §103(a)

Claims 15 - 34 stand rejected under 35 U.S.C. §103(a) as unpatentable over Muller et al. (WO 97/07239, the foreign equivalent to the '091 patent) in view of Wan et al., *Analytical Biochemistry*, Vol.223: 7-12 (1994).

Applicants note that the Examiner's reasons for this rejection are identical to the reasons underlying the obviousness-type double patenting issues discussed above; accordingly, Applicants comments above are applicable here as well.

In view of the amendments and foregoing remarks, reconsideration and allowance of the claims as amended are respectfully requested.

Respectfully submitted,



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